

PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PC/4-33522A/USN	FOR FURTHER ACTION		See Form PCT/PEA/416
International application No. PCT/EP2004/013412	International filing date (day/month/year) 25.11.2004	Priority date (day/month/year) 26.11.2003	
International Patent Classification (IPC) or national classification and IPC C07C237/20, C07D295/02, C07C237/24, C07C271/24, C07C323/29, C07C255/50, C07D319/18, C07D313/08, C07D307/79, C07D207/09, C07D333/08, A61P9/12, A61K31/165, A61K31/325, A61K31/44, A61K31/275, A61K31/357, A61K31/343, A61K31/5377, A61K31/402, A61K31/381			
Applicant NOVARTIS AG			
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 7 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> sent to the applicant and to the International Bureau a total of sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (Indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>			
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input checked="" type="checkbox"/> Box No. VI Certain documents cited</p> <p><input checked="" type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input checked="" type="checkbox"/> Box No. VIII Certain observations on the international application</p>			
Date of submission of the demand 02.09.2005		Date of completion of this report 18.10.2005	
Name and mailing address of the International preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized Officer Marie, G Telephone No. +49 89 2399- 	

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/EP2004/013412

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):*

Description, Pages

1-122 as originally filed

Claims, Numbers

1-37 as originally filed

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):

* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/EP2004/013412

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	5-8,17,18,20-28
	No: Claims	1-4,9-15,19,29, 30-38
Inventive step (IS)	Yes: Claims	-
	No: Claims	1-38
Industrial applicability (IA)	Yes: Claims	1-38
	No: Claims	-

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rule 70.10)

and /or

2. Non-written disclosures (Rule 70.9)

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item I

Basis of the opinion

The documents to which this communication refers are numbered in their order of appearance in the international search report.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Novelty (Article 33(2) PCT)

Preliminary remarks:

- a. The subject-matter of claims 9-11 also includes compounds according to claim 2 wherein R^2 is in the meta position and is unsubstituted lower alkoxy-lower alkoxy.
- b. In claim 19, R^2 can be an optionally substituted lower alkoxy-lower alkoxy (see third line of R^2 definition on *page 127*).

D2 discloses aminohydroxyaryl alkanoic acid amide compounds which are effective to inhibit renin activity. Amongst other novelty-destroying molecules, attention is drawn to some of the preferred embodiments of the present invention as claimed which are prepared in this document (see *RN numbers*), in particular molecules where R^2 or R^3 is halogenated and R^9 includes a cycloalkyl group.

Said document thus **anticipates the subject-matter of claims 1-4, 9-16, 19, 29, 30 and 32-38.**

Wood *et al.* (**D3**) discloses several molecules including aliskiren as effective renin inhibitors (see *fig. 1* and *abstract*). However, none of the molecules contain either a halogenated R^3 or a cycloalkylated R^9 .

Said document thus **anticipates the subject-matter of claims 1, 2, 9-11, 15, 16, 19, 29 and 32-38.**

Göschke *et al.* (**D4**) discloses several molecules including aliskiren as effective renin inhibitors (see *Table, pa.2738*). However, none of the molecules contain either a halogenated R³ or a cycloalkylated R⁹.

Said document thus **anticipates the subject-matter of claims 1, 2, 9-11, 15, 16, 19, 29 and 32-38.**

D5 anticipates the subject-matter of **at least claim 31** since it discloses synergistic combinations of pharmaceutical compounds, the first one being a renin inhibitor which structure falls under formula (I) and the second one being chosen amongst antidiabetic, hypolipidemic, anti-obesity and anti-hypertensive agents (see *claims*).

*N.B. Although document **D1** is highly relevant for the present subject-matter claimed, it will not be discussed before the International Authority. However, said document would be introduced for novelty (and inventive step, if the priority of the present application would not be valid) purposes during the regional phase before the EPO.*

2. Inventive step (Article 33(3) PCT)

In the remaining new subject-matter as claimed, a slight structural modification is defined in comparison to the compounds of **D2** having renin-inhibiting activity which comes within the scope of the customary practice followed by persons skilled in the art. The resulting effect of said slight modification(s) was foreseeable.

Insofar as no surprising and/or non-obvious effect has been demonstrated, no inventive step can be acknowledged.

3. Industrial applicability (Article 33(4) PCT)

Industrial applicability of the present invention is acknowledged.

Re Item VI

Certain documents cited

Certain published document

**INTERNATIONAL PRELIMINARY
REPORT ON PATENTABILITY
(SEPARATE SHEET)**

International application No.

PCT/EP2004/013412

Application No Patent No	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO 03/103653 (D1)	18/12/2003	11/06/2003	11/06/2002

Re Item VII

Certain defects in the application (form or content)

- 4.1** References to other documents may relate directly to the disclosure of the invention. If the matter the documents refer to is essential to satisfy the requirements of **Article 5 PCT**, this matter should be incorporated *expressis verbis* in the description because the patent specification should be self-contained regarding the essential features of the invention, i.e. capable of being understood without reference to any document.
As a consequence, the expression/sentence "...incorporated by reference..." from pages 28 and 122 should not be used (PCT Guidelines 4.26).

- 4.2** Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents **D2-D5** is not mentioned in the description, nor are these documents identified therein.

Re Item VIII

Certain observations on the international application (clarity)

- 5.1** The relative term "*lower*" in the field of organic chemistry does not have a generally accepted meaning with respect to the maximum number of carbon atoms. Such a term is ambiguous and therefore not suitable for clearly defining the subject-matter for which protection is sought. The definition given in the description for each substituent should have been included in the claims (PCT Guidelines 5.34).
- 5.2** The word "*spirit*" on page 122, last paragraph leads to doubt concerning the subject-matter claimed (PCT Guidelines 5.30).

- 5.3 The subject-matter of claims 3-8 is broader than the subject-matter of claim 1 because "*mono, di or tri-halo-substituted alkyl*" is broader than "*optionally halogenated lower alkyl*"
- 5.4 The subject-matter of claims 9-17 is broader than the subject-matter of claim 1 because the optional substitution by halogen(s) of lower alkoxy-lower alkoxy for R² is not mentioned.
- 5.5 "*Cycloalkoxy*" occurs twice in the definition of R² in claim 19.
- 5.6 The subject-matter of claim 21 is broader than the subject-matter of claim 1 to which it refers because R⁹ cannot be hydrogen (*page 130, line 1*) in claim 1 and "*halogenated alkyl*" (*page 130, line 1*) is broader than "*optionally halogenated lower alkyl*".
- 5.7 The subject-matter of claims 32, 33, 34 and 36 is not allowable because it refers to different independent claims whereas a dependent claim should only refer to one.